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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,401	02/27/2007	Seth Hallstrom	16785.10	8352

22913 7590 05/24/2011

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EXAMINER	
LIU, SAMUEL W	

ART UNIT	PAPER NUMBER
1656	

MAIL DATE	DELIVERY MODE
05/24/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/599,401	**Applicant(s)** HALLSTROM ET AL.	
	Examiner SAMUEL LIU	**Art Unit** 1656	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 12 May 2011 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): 112/2 rejection of claims 1, 2, 7 and 14.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *none*.
   Claim(s) objected to: *none*.
   Claim(s) rejected: *1,2,7 and 14*.
   Claim(s) withdrawn from consideration: *none*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/SAMUEL LIU/
Examiner, Art Unit 1656

/ANAND U DESAI/
Primary Examiner, Art Unit 1656

Continuation of 11. does NOT place the application in condition for allowance because: The 103(a) rejection of claims 1, 2, 7 and 14 by Schlag et al. and Hallstrom et al. is maintained.

The response filed 5/12/11 argues that reduced glutathione does not have an S-nitroso group in place of the thiol group (p.4). The response submits that Schlag et al. disclose the use of a "plurality [of] thiol nitrosated (i.e., S-nitroso) thiol-group-containing proteins, and that Schlag et al. do not teach/suggest the specific combination of "S-nitroso albumin" and "S-nitroso-glutathione". At best Schlag discloses a very broad genus of different combinations of S-nitroso proteins but fails to disclose a narrow species that includes the specific combination of S-nitroso albumin and S-nitroso glutathione (p.5, 1st and 3rd paragraphs). The secondary reference Hallstrom et al. do not teach/suggest said specific combination, but rather, merely identify the fact that both reduced glutathione (GSH) exist naturally in the body in specific ratios. Thus, the response infers that the Office fails to state a prima facie case of obviousness relative to the claims as amended and previously presented (see page 6 and 7). In addition, the response asserts that, even assuming for the sake of argument that Schlag, as asserted in the Office Action, suggests motivation of treating ischemia using a combination of N-nitroso proteins and GSH (age 6, 3rd paragraph).

Based on discussion of release of the active NO groups over a longer period of time referring to col.7, lines 25-33 of Schlag et al. (see page 7, 2nd paragraph, response), the response asserts that Schlag et al, teach away from instant invention with regard to potentiation of the NO-releaser of nitrosated serum albumin (S-NO-HAS, set forth in p.13, lines 9-13, Example 2, instant specification). The response asserts that the combination of 103 references Schlag et al. and Hallstrom et al. does not suggest instant combination of "S-nitroso albumin" and "S-nitroso glutathione", and thus infers that instant claims are not prima facie obvious over the combination of the103 references (see page 6, last paragraph to page 8, 2nd paragraph).
Further, at pages 8-9, the response discusses unexpected results shown in instant examples 1-3 (especially, page 9, lines 4-5), and asserted that, even if the combination of Schlag and Hallstrom renders claims 1-3 prima facie obvious, said unexpected results would rebut said obviousness (page 9, 2nd and 3rd paragraphs).

The applicants' arguments are found unpersuasive because of the reasons set forth in the interview summary mailed 5/12/11, the office action mailed 3/16/11 and the reasons below.

Claim 1 recites "reduced glutathione" NOT "S-nitroso-glutathione". It appears that the response misinterprets the claim.
The claim 1 open-ended language "comprising" allows for said "plurality" of S-nitroso-protein(s).

Schlag et al. have taught administering S-NO-HSA to a subject in need thereof (which meets the corresponding new limitation recited in the amended claim 1) for treating ischemia. The motivation of the combining use of S-NO-HAS with GSH is based on the fact that GSH serves as the first line of defense against ischemia tissue injury via reducing the level of detrimental O2- redial which directly causes the ischemia disease state. Although, the 103 references do not expressly teach the specific combination of S-NO-HAS with GSH, upon reading the 103 references, one of ordinary skill in the art would have known that the dynamic GSH level in vivo is insufficient and thus would have administered GSH to said subject suffering the ischemia with reasonable expectation of success; and thus, the combination of the 103 references' teachings, renders the claimed method prima facie obvious in the absence of unexpected result (see also page 5, the office action mailed 3/16/11).

It is of note that applicants have realized this "prima facie obvious" (see the above statement "even if the combination of Schlag and Hallstrom renders claims 1-3 prima facie obvious"). It appears that remaining issue regards the "unexpected results" asserted by the response.

Instant examples 1-3 are considered to be insufficient to provide evidence for supporting said "unexpected or surprising results". Nowhere in the specification has described said unexpected or surprising result(s). The use of GSH to treat ischemia state has been taught and suggested by Hallstrom et al. (see the 103 rejection and above). GSH is a compound routinely used by one of ordinary skill in the art as is evidenced by both references Schlag (suggesting use of GSH in general) and Hallstrom (suggesting use of GSH specifically for treatment of ischemia). Moreover, Schlag et al. have suggested that the mixture of nitrosated protein with non-nitrosated protein/polypeptide having free thiol group is particularly preferred (see the corresponding discussion in the rejection). Upon reading the references Schlag and Hallstrom, the "synergistic effect" (discussed at page 6, Finality mailed 3/16/11) would have been obvious to one of ordinary skill in the art; and thus, use of S-NO-HAS along with GSH for treating ischemia state would have rendered instant claims prima facie obvious in the absence any unexpected results.
Therefore, the 103 rejection is proper and maintained.

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